

Remarks

Claims 1-19 were pending in the subject application. Applicants gratefully acknowledge the Examiner's withdrawal of the rejections under 35 USC §102 over Richardson *et al.* (WO 01/06004) and under 35 USC §103 over Richardson *et al.* in view of Fend *et al.* Accordingly, claims 1-19 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Claims 1-6 and 8-19 are rejected under 35 USC §103(a) as obvious over Richardson *et al.* (WO 01/06004) in view of Gu *et al.* (U.S. Published Application No. 2003/0180737). In addition, claim 7 is rejected under 35 USC §103(a) as obvious over Richardson *et al.* (WO 01/06004) in view of Gu *et al.* (U.S. Patent Application No. 2003/0180737) and further in view of Fend *et al.* (1999). The Examiner asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to carry out first and second strand cDNA synthesis using the "single-pot" method of the Gu *et al.* publication when practicing the method of the Richardson *et al.* publication. Applicants respectfully traverse these grounds of rejection.

Applicants respectfully assert that the cited references, whether taken alone or in combination, do not teach or suggest the claimed invention. The Fend *et al.* reference, cited in regard to claim 7, does not cure the deficiencies of the Richardson *et al.* and Gu *et al.* publications. The Examiner asserts that it would have been obvious to adapt the method of the Richardson *et al.* publication so that the reverse transcription and amplification are carried out using the "single-pot" method of Gu *et al.* As the Examiner is aware, in order to establish a *prima facie* case of obviousness, it is necessary for the Patent Office to show that the ordinarily skilled artisan would have had some motivation to combine the cited references. *In re Geiger*, 2 USPQ2d 1276 (Fed. Cir. 1987). Applicants respectfully assert that the Examiner has not shown the requisite motivation to combine the teachings of the Richardson *et al.* and Gu *et al.* publications. In particular, the Examiner has not provided any evidence or showing that the method in the Richardson *et al.* publication is inefficient, or that it could be improved upon by combining the reverse transcription and amplification step. The ordinarily skilled artisan would not have looked to combine the teachings of the Richardson *et al.* and Gu *et al.* publications as there was no teaching or suggestion in

the art that such a combination would yield desirable results, or that it would even work at all. As the Examiner is undoubtedly aware, hindsight reconstruction of the prior art to arrive at Applicant's invention is not permissible. *In re Sponnoble*, 160 USPQ 237, 243 (CCPA 1969).

Moreover, the Examiner has not provided any evidence that the results obtained with Applicants' claimed invention were predictable from the cited publications or from the general knowledge of a person of ordinary skill in the art. The U.S. Supreme Court has indicated that a combination of elements is unlikely to be obvious when the combined elements yield unpredictable or unexpected results. *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007). Applicants respectfully assert that there are unexpected advantages and unpredictable results associated with Applicants' claimed invention that are not suggested in, or that could have been predicted from, the cited publications or the general knowledge of the ordinary artisan. Applicants' claimed invention is simpler and more efficient, and requires fewer amplification cycles, than methods known in the art at the time of Applicants' invention. There is nothing in the art that would lead an ordinarily skilled artisan to predict that Applicants' claimed invention would be more efficient or require fewer amplification cycles. In addition, Applicants' claimed invention solves problems that are not even addressed or recognized in the cited publications. For example, by comparison with the procedure in the Richardson *et al.* publication, the present invention avoids the need for rare restriction sites, and it allows for the inclusion of specific restriction sites for lambda cloning. Another advantage is that the production of complex products is minimized, due in part to the use of unique sequences in the heeled 5'-amplification and the heeled 3'-amplification primers which are absent from the genome being investigated. Moreover, while the procedure described in the Richardson *et al.* publication uses a single primer to amplify the products after reverse transcriptase and second strand synthesis, the present invention provides the significant advantage that two separate primers of unique sequence are used. In addition, Applicants' claimed invention not only provides greater amplification but also greater flexibility in use. For example, it readily allows the inclusion of specific restriction sites, for manufacturing subtracted normalized and enriched cDNA libraries, for fragmentation, and for use as probes on the microarrays and filters. It also allows the inclusion of specific restriction sites for lambda cloning, for the manufacture of single cell libraries. These are surprising and unexpected results that could not have been predicted from the teachings of the

Richardson *et al.* and Gu *et al.* publications. Thus, Applicants' claimed invention is not obvious over the cited publications. Accordingly, reconsideration and withdrawal of the rejections under 35 USC §103 is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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